

limitations of its parent claim and any intervening claims. It is respectfully submitted that claims 46 and 47 are allowable.

New claim 48 is directed to the subject matter of original claim 38, but written in method format.

It is brought to the Examiner's attention that counsel filed a Supplemental Information Disclosure Statement on November 17, 1999 in which the PCT Search Report and cited references in the counterpart PCT application were submitted for consideration. It is respectfully requested that this information be made of record in this application.

PRIOR ART REJECTIONS

Claims 1-3 and 8 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by U.S. Patent No. 3,964,482 to Gerstel.

Claims 1, 3, 8, 9, 13, 17, 18, 21, 29 and 45 were further rejected under 35 U.S.C. 102(e) as allegedly being anticipated by U.S. Patent No. 5,947,921 to Johnson.

Claims 1 and 7 were further rejected under 35 U.S.C. 102 as allegedly being anticipated by Ammonia Amplifies Nicotine, Study Confirms, by John Schwartz.

Claims 2 and 10-12 were rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Johnson, Gerstel and U.S. Patent No. 5,250,023 to Lee.

Claims 4-6, 14 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Johnson and U.S. Patent No. 5,427,585 to Bettinger.

The present invention is directed to a technique for enhancing the flux rate of a substance through (into or out of) a tissue whereby an outer layer of the tissue is breached to form at least one micropore therein, and by physically breaching the outer layer, access is gained to tissue structures in or beneath the outer layer to deliver an effective amount of flux enhancer that can act on those tissue structures which would not otherwise be possible without physically breaching the outer layer. The formation of the micropore (caused by physically breaching the tissue) before or simultaneous with the delivery of

the flux enhancer is a very important aspect of the present invention because it allows for the delivery of the flux enhancer beyond the surface of the tissue. Examples of tissue structures that are targeted by the flux enhancer are cells and capillaries in or beneath the stratum corneum, such as in the dermis. See page 11, lines 14-19 of the present application.

Independent claims 1 and 9 have been amended to emphasize this distinction. In particular, claim 1 has been amended to indicate that the flux enhancer is delivered into the tissue through at least one micropore made into an outer layer of the tissue so that the flux enhancer acts on tissue structures in or beneath the outer layer thereby increasing the flux rate of a substance through the tissue. Similar amendments are made to claim 9.

The term “micropore” has a defined meaning in the context of the claim language, and a definition appears in the present application at page 8, lines 6-16. The definition is made so as to distinguish a “micropore” formed by the defined “microporation” process versus an extremely small pore formed by an electroporation process. It is respectfully requested that consideration be given to the definitions of these terms in the claims.

Gerstel is directed to a drug delivery device featuring a reservoir containing a drug and a plurality of projections to penetrate the stratum corneum and allow the drug to be administered percutaneously. According to Gerstel, the sole “barrier” to moving the drug into the tissue is the stratum corneum, and once it is breached, no other flux enhancement acts are made. By contrast, the present invention is directed to moving substances across tissue structures in or beneath the outer layer of the tissue (or biological membrane) by physically breaching the outer layer to form a micropore therein and delivering an effective amount of a flux enhancer through the micropore so that the flux enhancer acts on tissue structures in or beneath the outer layer. Gerstel does not teach or suggest this aspect of the present invention.

Johnson is directed to a transdermal delivery technique whereby chemical enhancers are used to increase the solubility of the compound to be transported and/or lipid bi-layer solubility. Johnson employs non-physical breaching techniques as driving

forces for transport, such as mechanical or osmotic pressure, magnetic fields, electroporation or iontophoresis. Again, the present invention is different from Johnson because the present invention involves physically breaching the outer layer of the tissue to form a micropore therein in order to deliver flux enhancers into the micropore that act on tissue structures in or beneath the outer tissue layer. Johnson is not concerned with acting on tissue structures in or beneath an outer tissue layer, but rather is directed at getting compounds across the outer layer itself, and without physically breaching the outer layer.

The Schwartz article was applied against original claims 1 and 7. Schwartz, like Gerstel and Johnson, fails to teach or suggest delivering a flux enhancer through a micropore in an outer tissue layer (formed by physically breaching the outer tissue layer) so that the flux enhancer acts on tissue structures in or beneath the outer tissue layer.

The remaining rejections are against dependent claims based on combinations of the primary references to Johnson and Gerstel in combination with other references, such as Lee and Bettinger. No suggestion is made in these references to combine the teachings described therein with respect to the dependent claims. Moreover, it is respectfully submitted that the amendments to the independent claims 1 and 9 obviate these rejections because the various dependent claims should now be allowable in view of their dependency on claims 1 or 9.

An Information Disclosure Statement and applicable fee is filed concurrently herewith submitting a reference for consideration by the Examiner.

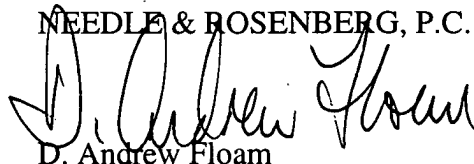
Based on the foregoing, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any questions or comments, he is

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cordially invited to telephone the undersigned so that the present application may receive a prompt Notice of Allowance.

Respectfully submitted,

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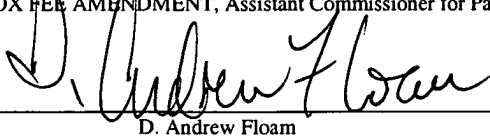


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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: BOX FEE AMENDMENT, Assistant Commissioner for Patents, Washington, D.C. 20231, on the date indicated below.



D. Andrew Floam

January 11, 2000

Date